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Influence of Gestational Age and Parental Education on Executive Functions of Children Born Very Preterm

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Abstract

Background: Children born very preterm (<32 weeks' gestational age; VPT) and/or very low birth weight (<1500 g; VLBW) are at high risk of deficits in executive functions, namely inhibition, working memory, and shifting. Both, gestational age and socioeconomic factors, such as parental education, are known to influence executive functions, with children born at lower gestational age and with lower educated parents displaying worse executive skills. This study aimed to investigate if maternal and paternal education moderated the relationship between gestational age and executive functions in VPT/VLBW children aged 8-12 years. It was hypothesised that the disadvantageous effect of low gestational age could be buffered more easily in families with higher educational background.

Methods: Sixty VPT/VLBW children born in the cohort of 1998-2003 were recruited. All children completed executive function tasks (inhibition, working memory, and shifting).

Results: There was a significant dose-response-relationship between gestational age and inhibition, with children being born at earlier gestational age showing worse inhibition. However, neither maternal nor paternal education moderated the relationship between gestational age and executive functions significantly.

Conclusion: Findings suggest that gestational age was more determining for executive functions of VPT/VLBW children than parental education. The disadvantageous effect of low gestational age was equal in children with higher and lower educated parents. However, the impact of gestational age and parental education on executive functions may differ depending on the socioeconomic spectrum of the study sample.

Keywords: Children born very preterm; Parental education; Inhibition; Working memory; Shifting

Abbreviations: VPT/VLBW: Very Preterm or Very Low Birth Weight

Introduction

Children born very preterm (<32 weeks of gestation; VPT) and/or with a very low birth weight (<1500 g; VLBW) are at high risk of deficits in executive functions [1]. Executive functions refer to cognitive processes that are important for purposeful and self-regulated behaviour [2], namely inhibition, working memory, and shifting [3]. Inhibition is defined as the ability to suppress prepotent responses or ongoing processes and avoid cognitive interference [3]. Working memory is considered as the capacity to maintain and process information during a short period of time [4]. Shifting refers to the ability to deliberately shift between mental tasks or sets [3]. In school-aged children, difficulties in inhibition, working memory, and shifting relate to problems in mathematics [5], reading and writing skills [6]. VPT/VLBW children at ages 8 to 12 years are shown to perform worse than full-term controls in inhibition, working memory, and shifting [7,8]. Furthermore, low gestational age and/or high rates of severe neonatal complications (e.g. haemorrhage, periventricular leukomalacia) are associated with poor inhibition, working memory, and shifting [9-11], with children being born at lower gestational age and/or exhibiting many complications displaying more executive problems later in life [1,7,11].

During the third trimester of pregnancy, the foetus' brain develops dramatically. Total brain volume increases 2.7-fold, cortical grey matter increases 4-fold, white matter increases 5-fold [12] and the cerebral cortex becomes folded [13]. Decreased cortical volume, less myelination [14] and reduced cortical surface area [15] have been observed in VPT/VLBW infants at term compared to same-aged full-term infants. The alterations in structural brain development were increased with reduced gestational age [16], suggesting a dose-response relationship between the degree of prematurity and the alteration in structural brain maturation.

The emergence of executive functions has been linked to the maturation of the prefrontal cortex [17], which exhibits a protracted period of postnatal maturation [18]. A peak in grey matter maturation in the prefrontal cortex occurs between the ages of 11 and 12 years, which corresponds to the age window where executive functions become increasingly specialised [19]. Executive functions are the latest maturing brain functions during development [20], therefore offering socioeconomic factors a large window of plasticity to affect the structural differentiation and functional capability of the prefrontal cortex [21]. Socioeconomic factors have been shown to relate to executive functions in healthy [20] and preterm-born children [1], with children from families with higher socioeconomic position performing better in executive functions. Some studies reported the influence of parental socioeconomic position on cognitive

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development to decline when children entered school [22], whereas other studies established a stable influence across childhood [23]. The socioeconomic position usually is measured as parental education, income or occupational status [23]. Of these three indicators, parental education is shown to be the best predictor of the children's cognitive outcome [24], possibly because it tends to be the most stable aspect of one's socioeconomic position over time [23]. In general, parental education may affect the extent to which parents can provide resources to their children (e.g. books and learning materials, monitoring of the child's activities, complexity of speech and vocabulary) or manage to recruit supporting social networks (i.e. social capital) [25].

The present study investigated whether maternal and paternal education moderated the relationship between gestational age and executive functions in VPT/VLBW children. It was hypothesised that the disadvantageous effect of early gestational age could be buffered more easily in families with higher educational background. The moderator effect was tested on a sample of VPT/VLBW children with no or mild neonatal cerebral lesions, as these children represent the majority of the preterm population [70%] [26].

Methods

This study reports on a subset of data from the NEMO (NEuropsychology und meMOry) research project at the Children's University Hospital in Bern, Switzerland. The NEMO project examines cognitive development and the effect of cognitive training in VPT/VLBW children and has been approved by the ethics committee of the Children's University Hospital in Bern. All children and caregivers provided informed written consent prior to participation, consistent with the Code of Ethics of the World Medical Association (Declaration of Helsinki).

Participants

The medical records of all VPT/VLBW children (<32 weeks gestational age and/or <1500 g birth weight) born in the cohort of 1998 to 2003 at the Children's University Hospital in Bern, Switzerland, were reviewed. Inclusion criteria were: (a) aged between 8 and 12 years; (b) maximal haemorrhage grade II; (c) maximal periventricular leukomalacia grade II; (d) no chronic illness potentially influencing development (e.g., congenital defects, cerebral palsy or epilepsy); (e) no medical problems potentially influencing development (e.g., meningitis, encephalopathy, traumatic brain injury); (f) no pervasive developmental disorders (e.g., autism). As this study is part of a large clinical trial examining the effect of cognitive training in VPT/VLBW children, only children with IQ>85 were included in order to avoid cognitive heterogeneity. According to their medical records, 247 children (92.5%) fulfilled the inclusion criteria. They were contacted by a letter including an information booklet for parents and children. After obtaining written consent from the caregivers, children were assessed individually by a trained neuropsychologist (B.R. or R.E.). Sixty-three children (25.50%) completed the neuropsychological assessment, but 3 children had to be excluded because IQ<85 (n=2; 3.17%) or refusal at assessment (n=1; 1.58%). Finally, 60 VPT/VLBW children, 27 girls (45%) and 33 boys (55%) were included in the analyses.

Assessment

To assess cognitive functions, well-known and standardised neuropsychological tests were employed. Raw scores were transformed into age-corrected scaled scores or index scores according to the respective test manual, with high scores reflecting better performance.

Inhibition was assessed using the first (colour naming task) and third condition (interference task) of the D-KEFS' Colour-Word Interference Test (Delis-Kaplan Executive Function System, D-KEFS [27]. In the colour naming task, the child was asked to name colour patches as fast as possible (no inhibitory load). In the interference task, the child had to name the ink colours of words printed in an incongruent ink as fast as possible (high inhibitory load). The measure of inhibition was the difference between the colour naming and interference tasks. *Working memory* was assessed using the digit span backwards task of the German version of the Wechsler intelligence scale for children (WISC-IV) [28]. The variable of interest was the maximum backward span attained. *Shifting* was assessed using the forth condition of the D-KEFS Trail Making Test (number-letter-switching; D-KEFS) [27]. The child was asked to connect numbers (1 to 16) and letters (A to P) by switching between connecting numbers in correct order as fast as possible (i.e. 1-A-2-B-3-C et cetera). *General intelligence* was assessed using the short form of the WISC-IV [28,29]. Full-scale IQ and index scores were calculated from scores on seven subtests of the original WISC-IV [29]. Processing speed and verbal comprehension was assessed to control for possible confounder variables. *Processing speed* was assessed using the processing speed index score of the short form of the WISC-IV [28,29]. *Verbal comprehension* was assessed using the verbal comprehension index score of the short form of the German version of the Wechsler intelligence scale for children [28,29]. *Socioeconomic status* was defined as maternal and paternal education level at the time when the neuropsychological assessment took place. No graduation was coded as 1, college as 2, college of higher education as 3, and university degree as 4. Information about the gestational age was collected from the children's neonatal medical records. It was measured in weeks and days based on the date of the last menstrual period and a prenatal ultrasound scan.

Statistical analyses

To test the study hypothesis, the moderator effect of maternal and paternal education on the relationship between gestational age and executive functions was analysed by means of hierarchical multiple regression using the Statistical Package for Social Sciences software for Windows, version 17 (SPSS, Chicago, Illinois). Statistical assumptions to conduct a moderator analyses with hierarchical regression are (a) normal distribution of the dependent variables and (b) the absence of multicollinearity effects [30]. In a sample of as many as 60 subjects, normal distribution of the dependent variables (i.e. executive functions performance) can be expected [31]. To

	Mean	*SD*	*Min*	*Max*
Age at assessment	10.01	1.50	8.03	12.97
Maternal education[1]	2.33	0.60	2	4
Paternal education[1]	2.57	0.87	2	4
Number of siblings	1.60	1.10	0	4
Gestational age (weeks)	29.80	2.20	24.71	33.71
Birth weight (grams)	1238.25	354.16	570	2060
IQ[2]	100.75	10.03	85	122
Processing speed[2]	99.48	13.08	66	134
Verbal comprehension[2]	102.20	9.64	87	124
Inhibition[3]	9.57	2.70	2	16
Working memory[3]	9.70	1.10	7	12
Shifting[3]	8.74	3.55	2	14

Note. 1. Scale of education: 1=no graduation, 2=college, 3=college of higher education, 4=university degree; 2. WISC-IV, short form (*M*=100, *SD*=15); 3. Scaled score (*M*=10, *SD*=3), a high scaled score indicates that the child exhibited good inhibition, good working memory or good shifting ability.

Table 1: Descriptive Data.

	1.	2.	3.	4.	5.	6.	7.	8.	9.	10.	11.	12.
1. Age	-											
2. Maternal education	-0.13	-										
3. Paternal education	-0.03	**0.41****	-									
4. Number of siblings	0.01	0.02	0.04	-								
5. Gestational Age	0.01	0.06	0.03	0.11	-							
6. Birth weight	-0.03	0.09	-0.05	0.15	**0.64****	-						
7. IQ	0.23	0.08	**0.36****	-0.24	0.12	0.05	-					
8. Processing speed	**0.34****	0.06	0.09	-0.13	0.07	0.02	**0.66****	-				
9. Verbal comprehension	0.03	-0.02	**0.47****	**-0.27***	**0.32***	0.01	**0.66****	0.14	-			
10. Inhibition	0.17	0.01	-0.03	0.14	**0.32***	0.20	-0.19	0.04	**-0.26***	-		
11. Working Memory	-0.25	-0.02	-0.15	-0.09	-0.03	-0.12	**0.39****	0.19	0.20	**-0.31***	-	
12. Shifting	**0.29***	0.08	0.24	0.05	0.24	0.17	**0.55****	**0.58****	0.17	0.10	0.05	-

Note. Two-tailed Pearson's correlation coefficients are presented. *=p<0.05, **=p<0.01

Table 2: Pearson correlations coefficients (r) between all variables.

Executive Function	*Step*	*Entered variables*	*b*	*SE b*	*ß*	*p*	*R^2*	*p of R^2 change*
Inhibition	Step 1	GA	0.39	0.16	0.31	0.01*		
		ME	-0.04	0.57	-0.01	0.94	0.10	0.05
		PE	-0.12	0.39	-0.04	0.77	0.10	0.05
	Step 2	GA×ME	0.35	0.43	0.13	0.42	0.11	0.42
		GA×PE	0.20	0.21	0.13	0.35	0.12	0.35
Working Memory	Step 1	GA	-0.01	0.02	-0.02	0.86		
		ME	-0.01	0.09	-0.02	0.88	0.01	0.97
		PE	0.03	0.06	0.07	0.63	0.01	0.87
	Step 2	GA×ME	-0.07	0.07	-0.17	0.36	0.02	0.36
		GA×PE	-0.03	0.03	-0.11	0.42	0.02	0.42
Shifting	Step 1	GA	0.38	0.21	0.23	0.08		
		ME	0.43	0.76	0.07	0.57	0.06	0.17
		PE	0.94	0.51	0.23	0.07	0.11	0.03
	Step 2	GA×ME	0.96	0.56	0.27	0.09	0.11	0.09
		GA×PE	0.22	0.27	0.10	0.44	0.12	0.44

Note. Hierarchical multiple regression of the moderator analyses is presented. GA=gestational age; ME=maternal education; PE=paternal education; GA×ME=product term (interaction); *B*=unstandardised regression weight; *SE B*=standard error of the unstandardised regression weight B; *ß*=standardised regression weight; *p*=level of exact significance; *R^2*=explained variance of the predictors in the criterion; *p* of *R^2 change*=level of exact significance of the increase in explained variance; *=p<0.05

Table 3: Moderator analyses of maternal education (ME) and paternal education (PE).

eliminate multicollinearity effects, gestational age and maternal as well as paternal education were centred [30]. Then, gestational age and maternal as well as paternal education were multiplied together to create the interaction term. Finally, gestational age and maternal as well as paternal education were entered into a hierarchical multiple regression (step 1, direct effect), followed by the interaction (step 2, moderator effect). In the case of a moderator effect, adding the interaction term would significantly increase the explained variance in the dependent variable (ΔR^2), in contrast to the variance already explained by the predictor and the moderator entered in the first step.

Results

All parents of the VPT/VLBW children graduated from school (Table 1) (mothers: 44 (73.3%) college degree, 12 (20%) degree of college of higher education, 4 (6.7%) university degree; fathers: 41 (68.3%) college degree, 4 (6.7%) degree of college of higher education, 15 (25%) university degree). The mean IQ of the children and the mean executive functions were in the normative range. Maternal education correlated positively with paternal education (r=0.41, p<0.01) (Table 2). As expected, processing speed, verbal comprehension and working memory, correlated significantly with IQ (processing speed: r=0.66, p<0.01; verbal comprehension: r=0.66, p<0.01; working memory: r=0.39, p<0.01). With respect to executive functions, inhibition correlated significantly with gestational age (r=0.32, p<0.01), whereas neither working memory (r=-0.03, p=0.84) nor shifting (r=0.24, p=0.07) correlated significantly with gestational age. None of the executive functions were significantly associated with maternal or paternal education (Table 2).

Moderator analyses with maternal and paternal education

Regarding *inhibition*, a total of 10% (p=0.05) of the variance in inhibition was explained by gestational age and maternal as well as paternal education (step 1, direct effect; Table 3). Gestational age predicted inhibition significantly (b=0.39, p<0.05), whereas there was no significant predictive value of maternal (b=-0.04, p=0.94) or paternal education (b=-0.12, p=0.77) on inhibition. The prediction of gestational age remained significant even if confounder variables were taken into account: age (b=0.39, p<0.05); sex (b=0.38, p<0.05); IQ (b=0.42, p<0.05); processing speed (b=0.40, p<0.05); and verbal comprehension (b=0.42, p<0.01). Adding the interaction term between gestational age and maternal education (ΔR^2=0.01, p=0.42) and the interaction term between gestational age and paternal education (ΔR^2=0.02, p=0.35) did not increase the explained variance in inhibition significantly (step 2, moderator effect).

Regarding *working memory*, a total of 1% (p=0.97) of the variance in working memory was explained by gestational age and maternal as well as paternal education. Neither gestational age (b=-0.01, p=0.86) nor maternal (b=-0.01, p=0.88) or paternal education (b=0.03, p=0.63) predicted working memory significantly. Adding the interaction term between gestational age and maternal education (ΔR^2=0.01, p=0.36) and the interaction term between gestational age and paternal education (ΔR^2=0.01, p=0.42) did not increase the explained variance in working memory significantly.

Regarding shifting, a total of 6% (p=0.17) of the variance in shifting was explained by gestational age and maternal education and a total of 11% (p<0.03) of the variance in shifting was explained by gestational age and paternal education. Neither gestational age (b=0.38, p=0.08) nor maternal (b=0.43, p=0.57) or paternal education (b=0.94, p=0.07) predicted shifting significantly. Adding the interaction term between gestational age and maternal education (ΔR^2=0.05, p=0.09) and the interaction term between gestational age and paternal education (ΔR^2=0.01, p=0.44) did not increase the explained variance in shifting significantly.

To summarize, neither maternal nor paternal education moderated the relationship between gestational age and executive functions, namely inhibition, working memory, and shifting (Table 3).

Discussion

The present study investigated whether maternal and paternal education moderated the relationship between gestational age and VPT/VLBW children's performance in inhibition, working memory, and shifting. Analyses revealed that gestational age predicted inhibition of VPT/VLBW children. Higher gestational age was significantly associated with better inhibition, even when possible confounder variables (age, sex, IQ, processing speed, and verbal comprehension) were taken into account. Being born at a higher gestational age seems to facilitate the emergence of inhibition, presumably because brain maturation is less affected by prematurity with increasing duration of pregnancy. This is plausible when considering the remarkable brain development in the last trimester of pregnancy [12]. Davis et al. [32] reported that even modest decreases in the duration of pregnancy can be associated with profound and lasting effects on neurodevelopment, indicating a dose-response-relationship between the degree of prematurity and changes in structural brain maturation [16].

Hence, the present data suggest that neither maternal nor paternal education were significant moderators on the relationship between gestational age and executive functions. Parental education had no statistically significant impact on executive functions of this VPT/VLBW sample. In contrast, research shows that VPT/VLBW children of less educated parents perform lower in cognitive tests than children of higher educated parents [33]. Carlson (2003) [34] suggested three parental factors to support a child's executive development: maternal sensitivity (responding adequately to the infant's signals), scaffolding (offering the child assis-tance in tasks beyond its current capability) and mind-mindedness (commenting on the child's thoughts and actions). Sensitive and mind-minded parents who support learning with scaffolding provide their child with experiences of successful interaction with the environment and effective self-regulation, which boosts executive development. Parents with low education are more likely to experience adverse social and physical conditions (e.g. crowded housing, pollution, high crime rates), daily problems as a consequence of occupational or material disadvantage and stressful life events (e.g. loss of employment, frequent household moves and lack of access to medical care) [25], all factors which substantially affect parent-child interactions in everyday life. The chronic stress associated with low socioeconomic position can lead to decreased quality of care-giving, for example reduced emotional warmth and sensitivity to a child's needs, harsh disciplinary style and sparse verbal communication [25]. However, in Switzerland, where the present data was collected, socioeconomic standards and education level are relatively high. Switzerland consists of a good welfare and health care system and a stable low unemployment rate (2.7-2.9%; State Secretariat for Economic Affairs SECO, July 2012). All parents of the reported VPT/VLBW children graduated from school, which is the case in about 92.7% of Swiss citizens (Swiss Federal Statistical Office, 2011). On the one hand, it might be that parental education did not influence the relationship between gestational age and executive functions in this sample because all VPT/VLBW children have relatively high educated parents and, therefore, the variance of socioeconomic background was rather small. Additionally, one could speculate that the influence of parental education on the child's executive functions may be weaker in Switzerland compared to countries with worse socioeconomic standards. On the other hand, the influence of parental education on children's cognitive performances can diminish during school age [22], since schooling might equalize the influence of socioeconomic differences across children. It might be that parental education did not relate to executive functions in the school-aged VPT/VLBW children of this study, because the time window where parental education has its strongest influence on children's executive functions has already passed.

As limitation, all parents of this study graduated from school, therefore representing the majority but not the whole educational spectrum of Switzerland. A second aspect is that education is a rather distal factor of the child's socio-familial environment. More proximal socioeconomic factors, such as the availability of stimulating materials, parental responsivity or complexity of speech, may explain more variance in the outcome than distal factors. Combining distal and proximal assessments of one's socioeconomic position may provide further insights into the fine mechanisms enabling socioeconomic factors to affect a child's cognitive development. Third, due to the restricted sample size (n=60) the power of the study decreases, whereas the chance of outliers increases [35]. To minimize these consequences, we used methodological (e.g., careful selection of sample, homogenous age groups concerning demographic and birth data) and statistical methods (e.g., centering the variables to avoid multicollinearity effects). However, studies with larger sample size are needed to give further insight into the relationship between socioeconomic status, gestational age and executive functions in VPT/VLBW children. A fourth aspect relates to the assessment of the three executive functions. Each of the three executive functions was measured using a single assessment task rather than a variety of tasks.

Findings suggest that gestational age was more determining for executive functions of the VPT/VLBW children than parental education. The disadvantageous effect of low gestational age was equal in children with higher and lower educated parents. However, the impact of gestational age and parental education on executive functions may differ dependent on the socioeconomic spectrum of the study sample.

Conflict of Interest

There are no conflicts of interest to declare.

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